WEST Search History

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DB=USPT,PGPB; PLUR=YES; OP=ADJ			
L6	l3 and L5	2	L6
L5	beta$1blocker	772	L5
L4	pindolol	1009	L4
L3	l1 and L2	171	L3
L2	gastrointestinal	27583	L2
L1	((514/415)!.CCLS.)	872	L1

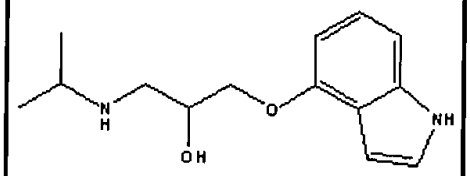
END OF SEARCH HISTORY

Enter a Chemical Name, CAS Number, Molecular Formula or Weight.
Use * for partial names (e.g. ben*).
Search here for free. For professional searching, use ChemINDEX.

Search

Pindolol [13523-86-9]

Synonyms: Barbloc; 2-Propanol, 1-(1H-indol-4-yloxy)-3-[(-methylethyl)amino]-; Pindolol; Visken;



Tools

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CAS RN Lookup

THE MERCK INDEX
NCI DATABASE

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VIEW LINKS
ADD COMPOUND
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ADD LINK

Formula	$C_{14}H_{20}N_2O_2$	Molecular Weight	248.3242
CAS RN	13523-86-9	Melting Point (°C)	
ACX Number	X1004427-8	Boiling Point (°C)	
Density		Vapor Density	
Refractive Index		Vapor Pressure	
Evaporation Rate		Water Solubility	
Flash Point (°C)		EPA Code	
DOT Number		RTECS	
Comments	Beta blocker, Vasodilator; 5-HT1A receptor antagonist		

More information about the chemical is available in these categories:

h che f e c b ge f c e

```
FILE 'HOME' ENTERED AT 19:05:05 ON 27 DEC 2001

=> FIL MEDLINE, BIOSIS, CA, CAPLUS, CAOLD, EMBASE, USPATFULL, PROMT
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                                                         ENTRY    SESSION
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FILE 'PROMT' ENTERED AT 19:05:16 ON 27 DEC 2001
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=> s 5ht1a antagonist or 5ht1a partial agonist
L1          159 5HT1A ANTAGONIST OR 5HT1A PARTIAL AGONIST

=> s 5ht1a (s) antagonist or 5ht1a (s) partial agonist
L2          435 5HT1A (S) ANTAGONIST OR 5HT1A (S) PARTIAL AGONIST

=> s ?pindolol
LEFT TRUNCATION IGNORED FOR '?PINDOLOL' FOR FILE 'PROMT'
L3        29438 ?PINDOLOL
Left truncation is not valid in the specified search field in the
specified file.  The term has been searched without left truncation.
Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID'
would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you
used a truncation symbol after a punctuation mark, the system may
interpret the truncation symbol as being at the beginning of a term.
Implied proximity is used in search fields indexed as single words,
for example, the Basic Index.

=> s gastrointestinal or gi or ulcer or duodenal or dyspepsia or irritable
bowel syndrome or ibs
```

```
L4       794460 GASTROINTESTINAL OR GI OR ULCER OR DUODENAL OR DYSPEPSIA OR
                IRRITABLE BOWEL SYNDROME OR IBS

=> s chemotherapy (s) nausea
L5        10475 CHEMOTHERAPY (S) NAUSEA

=> s l4 or l5
L6       803310 L4 OR L5

=> s l6 and l4
L7       794460 L6 AND L4

=> s l7 and l2
L8           17 L7 AND L2

=> dup rem
ENTER L# LIST OR (END):l8
DUPLICATE IS NOT AVAILABLE IN 'CAOLD'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L8
L9           14 DUP REM L8 (3 DUPLICATES REMOVED)

=> d l9 1-9 ibib, kwic

L9   ANSWER 1 OF 14  USPATFULL
ACCESSION NUMBER:        2001:150582  USPATFULL
TITLE:                   Compositions of optically pure (+) norcisapride
INVENTOR(S):             McCullough, John R., Hudson, MA, United States
                         Jerussi, Thomas P., Framingham, MA, United States
PATENT ASSIGNEE(S):      Sepracor Inc. (U.S. corporation)

                              NUMBER        KIND    DATE
                         ---------------- ------ --------
PATENT INFORMATION:      US 2001020031      A1   20010906
APPLICATION INFO.:       US 2001-809165     A1   20010316  (9)
RELATED APPLN. INFO.:    Continuation of Ser. No. US 2000-573423, filed on 18
                         May 2000, GRANTED, Pat. No. US 6242465 Continuation of
                         Ser. No. US 1998-123892, filed on 28 Jul 1998,
GRANTED,
                         Pat. No. US 6147093 Continuation-in-part of Ser. No.
US
                         1997-905941, filed on 5 Aug 1997, GRANTED, Pat. No. US
                         5877188 Division of Ser. No. US 1996-684753, filed on
                         19 Jul 1996, GRANTED, Pat. No. US 5739151
DOCUMENT TYPE:           Utility
FILE SEGMENT:            APPLICATION
LEGAL REPRESENTATIVE:    PENNIE & EDMONDS LLP, 1667 K STREET NW, SUITE 1000,
                         WASHINGTON, DC, 20006
NUMBER OF CLAIMS:        24
EXEMPLARY CLAIM:         1
LINE COUNT:              1069
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM   . . . The present invention relates to methods and compositions for
       treating central nervous system ("CNS") disorders, emesis, and
disorders
       associated with gastrointestinal motility dysfunction. In
       another aspect, this invention relates to metabolites of cisapride and
       optical isomers of such metabolites.
SUMM   . . . 5,057,525 and 5,137,896 (collectively "Van Daele") disclose
       N-(3-hydroxy-4-piperidenyl)benzamides including cisapride. These
```

compounds are said to stimulate the motility of the **gastrointestinal** system. Van Daele states that the cis and trans diastereomeric racemates of these compounds may be obtained separately by conventional. . .

SUMM . . . regard, it was discovered that a major site of production and storage of serotonin is the enterochromaffin cell of the **gastrointestinal** mucosa. It was also discovered that serotonin has a powerful stimulating action on intestinal motility by stimulating intestinal smooth muscle,. . .

SUMM [0008] Because of their modulation of the serotonin neuronal system in the **gastrointestinal** tract, many of the benzamide derivatives are often effective antiemetic agents and are commonly used to control vomiting during cancer **chemotherapy** or radiotherapy, especially when highly emetogenic compounds such as cisplatin are used (See: Costall et al., Neuropharmacology 26: 1321-1326, 1987).. . .

as the serotonin M-receptor (See: Clarke et al., Trends in Pharmacological Sciences 10: 385-386, 1989). Chemo- and radio-therapy may induce **nausea** and vomiting by the release of serotonin from damaged enterochromaffin cells in the **gastrointestinal** tract. Release of the neurotransmitter serotonin stimulates both afferent vagal nerve fibers (thus initiating the vomiting reflex) and serotonin receptors.

.

SUMM [0009] A second prominent action of the benzamide derivatives is in augmenting **gastrointestinal** smooth muscle activity from the esophagus to the proximal small bowel, thus accelerating esophageal and small intestinal transit as well. . .

SUMM [0013] Because of its activity as a prokinetic agent, cisapride may also be useful to treat **dyspepsia**, gastroparesis, constipation, postoperative ileus, and intestinal pseudo-obstruction.

SUMM [0014] **Dyspepsia** is a condition characterized by an impairment of the power or function of digestion that can arise as a symptom of a primary **gastrointestinal** dysfunction or as a complication due to other disorders such as appendicitis, gallbladder disturbances, or malnutrition. Gastroparesis is a paralysis. . .

SUMM . . . due to rapid first pass metabolism in the liver (See: Van Peer et al., in Progress in the Treatment of **Gastrointestinal** Motility Disorders: The Role of Cisapride. Proceedings of a Symposium in Frankfurt. November 1986. Johnson A. G. and Lux, G.. . .

SUMM . . . disease and such other conditions as may be related to the activity of (+) norcisapride as a prokinetic agent, e.g., **dyspepsia**, gastroparesis, constipation, post-operative ileus, and intestinal pseudo-obstruction. In addition, optically pure (+) norcisapride may be used to treat such conditions. . .

SUMM . . . conditions that may be related to the activity of (+) norcisapride as a prokinetic agent, including but not limited to **dyspepsia**, gastroparesis, constipation, and intestinal pseudo-obstruction. Moreover, optically pure (+) norcisapride may be used to treat these conditions while substantially reducing. . .

SUMM [0034] A further aspect of the present invention includes a method of treating a condition caused by **gastrointestinal** motility dysfunction in a human which comprises administering to a human in need of treatment for **gastrointestinal** motility dysfunction, a therapeutically effective amount of (+) norcisapride, or a pharmaceutically acceptable salt thereof, substantially free of its (-) stereoisomer. Conditions caused by **gastrointestinal** motility dysfunction in a human include, but are not limited to,

gastro-esophageal reflux disease, **dyspepsia**, gastroparesis, constipation, post-operative ileus, and intestinal pseudo-obstruction.

SUMM [0035] Furthermore, the present invention includes a pharmaceutical composition for treating a condition caused by **gastrointestinal** motility dysfunction in a human, which comprises (+) norcisapride, or a pharmaceutically acceptable salt thereof, substantially free of its (-).

. .

SUMM [0042] The term "adverse effects" includes, but is not limited to, **gastrointestinal** disorders such as diarrhea, abdominal cramping, and abdominal grumbling; tiredness; headache; cardiac depression; increased systolic pressure; increased heart rate; neurological. . .

SUMM . . . terms "eliciting an antiemetic effect" and "antiemetic therapy" as used herein mean providing relief from or preventing the symptoms of **nausea** and vomiting induced spontaneously or associated with emetogenic cancer **chemotherapy** or irradiation therapy.

SUMM [0045] The term "treating a condition caused by **gastrointestinal** motility dysfunction" as used herein means treating the symptoms and conditions associated with this disorder which include, but are not limited to, gastroesophageal reflux disease, **dyspepsia**, gastroparesis, constipation, postoperative ileus, and intestinal pseudo-obstruction.

SUMM [0046] The term "prokinetic" as used herein means the enhancement of peristalsis in, and thus the movement through the **gastrointestinal** tract.

SUMM [0048] The term "**dyspepsia**" as used herein means a condition characterized by an impairment of the power or function of digestion that can arise as a symptom of a primary **gastrointestinal** dysfunction or as a complication due to other disorders such as appendicitis, gallbladder disturbances, or malnutrition.

DETD [0083] **5HT1A** Receptor Activity Receptor selection and amplification technology (R-SAT) was used (Receptor Technologies Inc., Winooski, Vt.) to determine potential agonist and/or **antagonist** activity of racemic norcisapride, cisapride and their enantiomers on cloned human serotonin 5-HT.sub.1A receptor subtypes expressed in NIH 3T3 cells. . .

CLM What is claimed is:

1. A method of treating or preventing a disorder caused by **gastrointestinal** motility dysfunction in a human which comprises administering to said human a therapeutically effective amount of (+) norcisapride, or a. . .

3. The method of claim 1, wherein said disorder is **dyspepsia**.

L9 ANSWER 2 OF 14 USPATFULL

ACCESSION NUMBER: 2001:112329 USPATFULL

TITLE: Octahydrobenzo[f]quinoline-based receptor agonists and antagonists

INVENTOR(S): Froimowitz, Mark, Newton, MA, United States
Jacob, James N., Saunderstown, RI, United States

PATENT ASSIGNEE(S): The Board of Governors for Higher Education, Providence, RI, United States (U.S. corporation)
The State of Rhode Island and Providence Plantations., Providence, RI, United States (U.S. state government)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6262064	B1	20010717

APPLICATION INFO.: US 1999-237390 19990126 (9)
RELATED APPLN. INFO.: Continuation of Ser. No. US 1996-666286, filed on 26 Sep 1996, now patented, Pat. No. US 5863928
Continuation of Ser. No. WO 1993-US11302, filed on 19 Nov 1993
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Huang, Evelyn Mei
LEGAL REPRESENTATIVE: Hamilton, Brook, Smith & Reynolds, P.C.
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 1196
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . composition is a composition with a binding affinity for a receptor, wherein said composition can act as an agonist, an **antagonist** or a mixed agonist/**antagonist** to the receptor. Examples of receptors, for which the compositions of this invention are useful, include D2, D4, 5HT1, **5HT1A**, 5HT2, .alpha.1 and .alpha.2 receptors.
DETD . . . Binding was then terminated by dilution of the assay with a cold buffer, followed by rapid vacuum filtration onto Whatman **GI** /C filters that were presoaked in 0.1% polyethylene imine for at least 3 hours. Radioactivity trapped onto the filters was determined. . .

L9 ANSWER 3 OF 14 CA COPYRIGHT 2001 ACS DUPLICATE 1
ACCESSION NUMBER: 133:247090 CA
TITLE: The putative 'silent' 5-HT1A receptor antagonist, WAY 100635, has inverse agonist properties at cloned human 5-HT1A receptors
AUTHOR(S): Cosi, C.; Koek, W.
CORPORATE SOURCE: Division de Neurobiologie II, Centre de Recherche Pierre Fabre, Castres, 80106, Fr.
SOURCE: Eur. J. Pharmacol. (2000), 401(1), 9-15
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 18
REFERENCE(S): (1) Assie, M; Eur J Pharmacol 1996, V304, P15 CA
(2) Barr, A; J Biol Chem 1997, V272(52), P32979 CA
(3) Costa, T; Mol Pharmacol 1990, V37, P383 CA
(4) Costa, T; Mol Pharmacol 1992, V41, P549 CA
(5) Fargin, A; J Biol Chem 1989, V264, P14848 CA
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Agonist binding to G protein-coupled receptors induces the formation of a receptor-G protein complex and subsequent GDP/GTP (GDP/GTP) exchange. Some receptors, however, form receptor-G protein complexes and promote GDP/GTP exchange even when not occupied by agonists. Such receptors preferentially activate pertussis toxin-sensitive G proteins (i.e., **Gi**/Go), and the interactions of receptors and G proteins are affected by monovalent cations (most notably Na+), both in the occupied and unoccupied state. We investigated the effects of Na+ on the intrinsic activity of 5-hydroxytryptamine1A (5-HT1A) receptor ligands, measured as maximal effect (EMAX), using guanosine 5'-0-(3-[35S]thio)-triphosphate ([35S]GTP.gamma.S) binding to membranes prepd. from human epithelioid carcinoma (HeLa) cells, expressing 500 fmol/mg protein of cloned human

5-HT1A receptor (HA7 cells). A decrease of the NaCl concn. decreased the maximal effect of serotonin, increased basal [35S]GTP.gamma.S binding, and
increased the neg. intrinsic activity of spiperone and

N-2-[4-(2-methoxyphenyl)-1-piperazinyl]-N-(2-pyridinyl)cyclohexanecarboxamide (WAY 100635). This ability of WAY 100635 to decrease basal [35S]GTP.gamma.S binding was antagonized by (s)-N-tert-butyl-3-(4-(2-methoxyphenyl)piperazine-1-yl)-2-phenylpropanamide ((s)-WAY 100135) (pA2=7.77). Further, WAY 100635 was able to antagonize carboxamidotryptamine (5-CT)-stimulated [35S]GTP.gamma.S binding with a pA2 of 9.9, in std. NaCl conditions, and of 9.7, in the absence of NaCl. Changes in membrane concn. did not affect the ability of WAY 100635 to decrease [35S]GTP.gamma.S binding. WAY 100635 did not affect basal [35S]GTP.gamma.S binding to membranes from untransfected HeLa cells. Pertussis toxin (200 ng/mL) prevented WAY 100635 and spiperone to decrease
[35S]GTP.gamma.S binding, showing that their effects were mediated by G proteins of the **Gi**/Go family. In conclusion, the constitutive and stimulated activity of human 5-HT1A receptors expressed in HA7 cells is sodium-dependent, which allowed to confirm the 5-HT1A inverse agonist properties of spiperone, and to show that WAY 100635 is an inverse agonist
at 5-HT1A receptors that inhibits basal [35S]GTP.gamma.S binding to a lesser extent than spiperone. [35S]GTP.gamma.S binding to membranes from HA7 cells under low NaCl conditions appears to be esp. suitable to evidence and pharmacol. analyze the inverse agonist properties of 5-HT1A receptor ligands.

ST WAY100635 sodium **5HT1A** receptor **antagonist**

L9 ANSWER 4 OF 14 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 1999:850552 PROMT
TITLE: AstraZeneca unveils promising portfolio with 57 NCEs.
SOURCE: Marketletter, (20 Dec 1999) .
ISSN: 0951-3175.
PUBLISHER: Marketletter Publications Ltd.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 1182
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX The . . . is now focusing on seven therapeutic areas, is confident that it will be the world's number one in four markets: **gastrointestinal**; cardiovascular; oncology; and pain control. It is also optimistic about its respiratory program, where it aims to maintain its number. . .

Cardiovascular	
ZD6169	K+ channel opener
ZD7851/9720	OSC inhibitors
ZD1611/4054	Endothelin A antagonists
Gastrointestinal	
ropivacaine gel	Inflammatory bowel disease
PTH	Osteoporosis
Oncology	
ZD2767/9063	Antibody-directed enzyme prodrugs
ZD4190	VTK
ZD9481	Tyrosine kinase inhibitor
ZD0101	Anti-angiogenic
ZD3980	Anti-androgen
Respiratory	

rofleponide	Asthma				
TH2 project	Asthma				
Mast. . .					
NEW . . .	Thromb inhibitor(oral)	Thrombosis	III	2Q 2001	2Q 2001
H376/95	Thromb inhibitor(oral)	Prev of stroke	II	4Q 2003	4Q 2003
AR-C 69931	P2T **antagonist** (iv)	TBD	II	>2002	>2002
AR-C 126532	P2T antag(oral)	Arterial thromb	I	2005	2005
H327/86	Immunomodulator	TBD	II	>2002	>2002
AR-H039242	PPAR agonist	Insulin resistance	II	2003	2003
ZD4927	Factor Xa inhibitor	Thrombosis	I	>2002	>2002
H409/22	NPY **antagonist**	TBD	II	>2002	>2002
H345/52	Class III antiarryth(iv)	TBD	II	>2002	>2002
AR-H050642	Class III antiarryth(oral)	Atrial fibr	PC	2005	2005
Atacand/HTCZ	Angio II antag	Hypertension	Filed		
ZD0947	K+ channel opener	Urin incontin	I	>2002	>2002
Gastrointestinal					
esomeprazole	Acid pump inhib	Acid-related **GI**	Filed		
mosapride	5HT modulator	**Dyspepsia**	II	TBD	TBD
RAPID	Rev acid pump inhib	Acid-related **GI**	I	2004	2004
rofleponide	Topical steroid	**IBS**	PC	2004	2004
Helicobac	Vaccine	Helico eradicat	PC	2007	2007
Helicobac	Oral treatment	Helico eradicat	PC	2007	2007
Oncology					
Faslodex	Antiestrogen	Breast cancer. . .	opioid Acute/chronic pain	PC	
Oral glycine	NMDA antag	Neuropathic pain	PC		
CNS					
Zendra	GABA modulator	Stroke	III	4Q 2001	1Q 2001
AR-R15896	NMDA **antagonist**	Stroke	II	3Q 2002	3Q 2002
NXY-059	Radical scavenger	Stroke	II	3Q 2002	3Q 2002
NAD299	**5HT1A antagonist**	Anx/depression	II	>2002	>2002
AR-A2	5HT1B **antagonist**	Anx/depression	PC	>2002	>2002
remacemide	NMDA **antagonist**	Epilepsy	III	>2002	>2002
		Parkinson's disease	II	>2002	>2002
		Huntington's chorea	III	3Q 2001	3Q 2001

Infection
AZD2563 Oxazolidinone Gram-positive infects. . .

L9 ANSWER 5 OF 14 USPATFULL

ACCESSION NUMBER:	1999:24695 USPATFULL
TITLE:	Method of treatment for malaria utilizing serotonin receptor ligands
INVENTOR(S):	McConnell, Bruce, Albuquerque, AZ, United States Locher, Christopher P., San Francisco, CA, United States
PATENT ASSIGNEE(S):	The University of Hawaii, Honolulu, HI, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5874477		19990223	
APPLICATION INFO.:	US 1994-289379		19940812	(8)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	MacMillan, Keith D.
LEGAL REPRESENTATIVE:	Gray, Cary, Ware & Freidenrich, LLP, Reiter, Stephen E., Kleinsmith, David F.
NUMBER OF CLAIMS:	14
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT:	645

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . use of many existing anti-malaria drugs because of the side effects they produce in patients. For example, chloroquine can cause **gastrointestinal** disturbances, visual disturbances, irreversible damage to the retina, skin reactions, hair loss and hair depigmentation.

Furthermore, chloroquine must be used. . .

DETD . . . constant less than 10 nanomolar. Thus, while both ketanserin and spiperone (5HT2 identifying compounds) can be shown to bind to **5HT1a** receptors, they do not qualify as identifying ligands for the **5HT1a**, owing to a dissociation constant between 10 and 1000 nM for **5HT1a**. The definition of any chemical compound as an anti-malarial will be established by the ability of this compound to compete. . . ligand and anti-malarial, regardless of whether the actual functional receptor in anti-malarial activity can or cannot be established unequivocally as **5HT1a**, 5HT2 (a or b) or 5HT1c, subsequently. While any compound displacing a radioligand from the receptor with medium or high affinity qualifies as a ligand, its qualification as an anti-malarial candidate through further demonstration of its possible agonist, **partial agonist** or **antagonist** activity is supportive, but not necessary.

DETD . . . subtype sites, i.e. the ability to compete with any subtype-identifying compound, rather than to its actual function as agonist or **antagonist** at 5HT receptor subtype site. It should be recognized that the 5HT receptors operating in any anti-malarial system involving erythrocytes. . . of the identifying radioligand. Such binding assays have indicated that 8-hydroxy-DPAT and 5-methoxy-N, N-dimethyltryptamine (DMT) are identifying ligands for the **5HT1a** serotonin receptor subtype and ketanserin and spiperone are identifying ligands for the 5HT2 (a or b) and 5HT1c receptor subtypes.

DETD TABLE I

50%
PARASITE

SEROTONIN RECEPTOR	RECEPTOR SPECIFICITY	LIGAND FUNCTION	GROWTH INHIBIT..sup.(1) CONC. OF LIGAND IC.sub.50.sup.(2) (.mu.g/ml)	CPM's
8-hydroxy DPAT(1).sup.(3)	**5HT1a**	Agonist	0.125	900
DOI(9).sup.(4)	5HT2	Agonist	0.250	2055
2C-B(9).sup.(5)	5HT2	Agonist	0.500	1678
Serotonin	**5HT1a**,5HT2, a,b,c	Agonist	>10	(>4000) 0
Spiperone	5HT2, **5HT1a**	**Antagonist**	1.25	2591
Ritanserin	5HT2	**Antagonist**	2.50	2913
Ketanserin	5HT2	**Antagonist**	5.00	1592
DMT.sup.(6)	5HT2	Agonist	.gtoreq.10	(>4000) 0

##STR19##

where Control CPM (from 3 wells w/o drug) = 3977 CPM

Background. . .

DETD To quantitate the physiological response of malaria parasites to serotonin receptor (**5HT1a** and 5HT2) ligands, a patch-clamp technique can be used to (1) identify and locate the actual receptor within a lysis. . . remnant of the invaginated erythrocyte membrane that encloses the parasite; (2) characterize the basis of the parasite's physiological response to **5HT1a** and 5HT2 agonists; (3) characterize the transport properties of these receptors and ascribed a functional definition, i.e., nutrient permeable channel. . . 15, 1993); and (4) identify the mechanism of action of serotonin receptor ligands on the malaria parasite, i.e., agonist or **antagonist**.

L9 ANSWER 6 OF 14 USPATFULL

ACCESSION NUMBER: 1999:12937 USPATFULL

TITLE: Octahydrobenzo[f]quinoline-based receptor agonists and antagonists

INVENTOR(S): Froimowitz, Mark, Newton, MA, United States
Jacob, James N., SaundersTown, RI, United States

PATENT ASSIGNEE(S): The Board of Governors for Higher Education the State of Rhode Island and Providence Plantation., Providence, RI, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5863928		19990126	
	WO 9514006		19950526	##STR1##
APPLICATION INFO.:	US 1996-666286		19960926	(8)
	WO 1993-US11302		19931119	
			19960926	PCT 371 date
			19960926	PCT 102(e) date

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Huang, Evelyn
LEGAL REPRESENTATIVE: Hamilton, Brook, Smith & Reynolds, P.C.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 1250
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . composition is a composition with a binding affinity for a receptor, wherein said composition can act as an agonist, an **antagonist** or a mixed agonist/**antagonist** to the receptor. Examples of receptors, for which the compositions of this invention are useful, include D2, D4, 5HT1, **5HT1A**, 5HT2, .alpha.1 and .alpha.2 receptors.
DETD . . . Binding was then terminated by dilution of the assay with a cold buffer, followed by rapid vacuum filtration onto Whatman **GI** /C filters that were presoaked in 0.1% polyethylene imine for at least 3 hours. Radioactivity trapped onto the filters was determined. . .

L9 ANSWER 7 OF 14 CA COPYRIGHT 2001 ACS DUPLICATE 2
ACCESSION NUMBER: 128:294709 CA
TITLE: Heterocyclyloxyalkanamines having effects on serotonin-related systems
INVENTOR(S): Hibschman, David J.; Krushinski, Joseph H., Jr.; Rasmussen, Kurt; Rocco, Vincent P.; Schaus, John M.; Thompson, Dennis C.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 65 pp. Cont.-in-part of U.S. Ser. No. 373,823, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5741789	A	19980421	US 1995-467434	19950606
CN 1178530	A	19980408	CN 1996-192598	19960111
US 6172073	B1	20010109	US 1998-49837	19980327

PRIORITY APPLN. INFO.: US 1995-373823 B2 19950117
US 1995-467434 A3 19950606
OTHER SOURCE(S): MARPAT 128:294709
ST heterocyclyloxyalkanamine prepn serotonin 1A antagonist; serotonin 1A antagonist reuptake inhibitor heterocyclyloxyalkanamine; antidepressant heterocyclyloxyalkanamine prepn; nicotine withdrawal treatment heterocyclyloxyalkanamine prepn; indolyloxyalkanamine prepn **5HT1A antagonist**; quinolinyloxyalkanamine prepn **5HT1A antagonist**

IT **Gastrointestinal** motility
(treatment of disorders; prepn. of heterocyclyloxyalkanamines as serotonin 1A antagonists and reuptake inhibitors)

L9 ANSWER 8 OF 14 USPATFULL

ACCESSION NUMBER:	1998:154132 USPATFULL
TITLE:	Recombinant expression vectors for expression of heterologous proteins
INVENTOR(S):	Pausch, Mark H., Robbinsville, NJ, United States Ozenberger, Bradley A., Yardley, PA, United States Hadcock, John R., Mount Holly, NJ, United States Price, Laura A., Langhorne, PA, United States Kajkowski, Eileen M., Ringoes, NJ, United States Kirsch, Donald R., Princeton, NJ, United States Chaleff, Deborah T., Pennington, NJ, United States
PATENT ASSIGNEE(S):	American Cyanamid Company, Madison, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5846819		19981208
APPLICATION INFO.:	US 1995-472045		19950606 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1994-195729, filed on 14 Feb 1994		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Walsh, Stephen		
ASSISTANT EXAMINER:	Basham, Daryl A.		
LEGAL REPRESENTATIVE:	Matthews, Gale F.		
NUMBER OF CLAIMS:	14		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	44 Drawing Figure(s); 28 Drawing Page(s)		
LINE COUNT:	2790		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD Expression of the human **5HT1a** serotonergic receptor. The gene encoding the human **5HT1a** receptor is modified to add the first 14 amino acids of the yeast Ste2 protein, cloned into the expression plasmid. . . grown in medium containing galactose to induce receptor expression, fractioned and tested for receptor activity by binding of the radiolabelled **antagonist** .sup.3 H-spiperone. Saturation binding demonstrates that the receptor is expressed at high levels (B.sub.max =3.2 pmol/mg protein) and that it. . .

DETD Two chimeric receptor genes are engineered; in pCH17, sequences encoding the N-terminus including the first two transmembrane domains of the **5HT1a** receptor are replaced with the corresponding sequences of the Ste2 receptor, and in pCHI18, these Ste2 sequences are added directly to the N-terminus of the **5HT1a** receptor to create a novel nine-transmembrane-domain receptor (FIG. 4). Strains expressing these receptors are examined for binding of radiolabelled ligand. Both receptors demonstrate specific binding of the 5HT receptor **antagonist** .sup.3 H-spiperone (FIG. 4). Replacement of the first two transmembrane domains with those of an unrelated receptor does not apparently. . .

DETD . . . of CCK antagonists make them excellent candidates for treatment of pancreatitis, pancreatic cancer, biliary colic, disorders of gastric emptying, and **irritable bowel syndrome**.
CCK antagonists reverse the development of satiety and might be useful in improving appetite in anorectic patients or others that. . .

DETD 6. Wank, S. A., J. R. Pisenga, and A. de Weerth. 1992. Brain and **gastrointestinal** cholecystokinin receptor family: Structure and function. Proc. Natl. Acad. Sci. USA 89: 8691-8695.

DETD . . . and S. Seino. 1992. Cloning and functional characterization of a family of human and mouse somatostatin receptors expressed in brain, **gastrointestinal** tract, and kidney. Proc. Natl. Acad. Sci. USA 89: 251-255.

DETD . . . and S. Seino. 1992. Cloning and functional characterization of a family of human and mouse somatostatin receptors expressed in brain, **gastrointestinal** tract, and kidney. Proc. Natl. Acad. Sci. USA 89: 251-255.

L9 ANSWER 9 OF 14 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:13135 BIOSIS
DOCUMENT NUMBER: PREV199900013135
TITLE: Serotonin depresses excitatory synaptic transmission and depolarization-evoked Ca2+ influx in rat basolateral amygdala via 5-HT1A receptors.
AUTHOR(S): Cheng, Li-Ling; Wang, Su-Jane; Gean, Po-Wu (1)
CORPORATE SOURCE: (1) Dep. Pharmacol., Coll. Med., Natioanl Cheng-Kung Univ.,
Tainan City 701 Taiwan
SOURCE: European Journal of Neuroscience, (June, 1998) Vol. 10, No.
6, pp. 2163-2172.
ISSN: 0953-816X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB. . . pertussis toxin pretreatment did not affect the depressing effect of
5-HT suggesting that it is not mediated through activation of **Gi** /o protein-coupled K+ conductance. The sensitivity of postsynaptic neurons
to glutamate receptor agonist was unaltered by the 5-HT pretreatment. In addition,. . . action. The effect of 5-HT was mimicked by the selective
5-HT1A agonist 8-hydroxy-dipropylaminotetralin (8-OH-DPAT) and was blocked
by the selective **5HT1A antagonist** 1-(2-methoxyphenyl)-4(4-(2-phthalimido)butyl)piperazine oxadiazol-3-yl)methyl)phenyl)methanesulphonamide. In contrast, the selective 5-HT2 receptor **antagonist** ketanserin failed to affect the action of 5-HT. The effects of 5-HT and 8-OH-DPAT on the high K+-induced increase in. . . concentration-dependent manner. The effect of 5-HT was completely abolished in slices pretreated with Rp-cyclic adenosine 3',5'-monophosphothioate (Rp-cAMP), a regulatory site **antagonist** of protein kinase A, suggesting that 5-HT may act through a cAMP-dependent
mechanism. Taken together, these results suggest that functional. . .

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	125.56	125.71

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.56	-0.56

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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 14, 2001 (20011214/UP).

=> file home
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.00     125.71

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                     0.00      -0.56

FILE 'HOME' ENTERED AT 19:17:55 ON 27 DEC 2001

=> FIL MEDLINE, BIOSIS, CA, CAPLUS, CAOLD, EMBASE, USPATFULL, PROMT
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.75     126.46

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                     0.00      -0.56

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FILE 'PROMT' ENTERED AT 19:20:42 ON 27 DEC 2001
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=> s racemic pindolol
L10         100 RACEMIC PINDOLOL
```

```
=> s racemic (s) pindolol
L11         255 RACEMIC (S) PINDOLOL

=> d his

     (FILE 'HOME' ENTERED AT 19:05:05 ON 27 DEC 2001)

     FILE 'MEDLINE, BIOSIS, CA, CAPLUS, CAOLD, EMBASE, USPATFULL, PROMT'
     ENTERED AT 19:05:16 ON 27 DEC 2001
L1           159 S 5HT1A ANTAGONIST OR 5HT1A PARTIAL AGONIST
L2           435 S 5HT1A (S) ANTAGONIST OR 5HT1A (S) PARTIAL AGONIST
L3         29438 S ?PINDOLOL
L4        794460 S GASTROINTESTINAL OR GI OR ULCER OR DUODENAL OR DYSPEPSIA OR
I
L5         10475 S CHEMOTHERAPY (S) NAUSEA
L6        803310 S L4 OR L5
L7        794460 S L6 AND L4
L8            17 S L7 AND L2
L9            14 DUP REM L8 (3 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 19:17:14 ON 27 DEC 2001

     FILE 'HOME' ENTERED AT 19:17:55 ON 27 DEC 2001

     FILE 'MEDLINE, BIOSIS, CA, CAPLUS, CAOLD, EMBASE, USPATFULL, PROMT'
     ENTERED AT 19:20:42 ON 27 DEC 2001
L10          100 S RACEMIC PINDOLOL
L11          255 S RACEMIC (S) PINDOLOL

=> s l4 and l11
L12            2 L4 AND L11

=> dup rem
ENTER L# LIST OR (END):l12
DUPLICATE IS NOT AVAILABLE IN 'CAOLD'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L12
L13            2 DUP REM L12 (0 DUPLICATES REMOVED)

=> d l13 1-2 bib, ab, kwic

L13  ANSWER 1 OF 2  USPATFULL
AN      2001:231308  USPATFULL
TI      Methods of treating and preventing attention deficit disorders
IN      Jerussi, Thomas P., Framingham, MA, United States
        Senanayake, Chrisantha H., Shrewsbury, MA, United States
        Fang, Qun K., Wellesley, MA, United States
PA      Sepracor, Inc., Marlbourgh, MA, United States (U.S. corporation)
PI      US 6331571          B1   20011218
AI      US 1999-372158           19990811 (9)
PRAI    US 1998-97665       19980824 (60)
        US 1998-99306       19980902 (60)
DT      Utility
FS      GRANTED
EXNAM   Primary Examiner: Jarvis, William R. A.
LREP    Pennie & Edmonds LLP
CLMN    Number of Claims: 4
ECL     Exemplary Claim: 1
DRWN    No Drawings
LN.CNT 1900
```

AB Methods are disclosed for the treatment and prevention of affective disorders with racemic or optically pure sibutramine metabolites and pharmaceutically acceptable salts, solvates, and clathrates thereof.

SUMM Sibutramine is rapidly absorbed from the **gastrointestinal** tract following oral administration and undergoes an extensive first-pass metabolism that yields the primary metabolites, desmethylsibutramine and didesmethylsibutramine, shown below.. . .

SUMM The invention further encompasses methods of using and pharmaceutical compositions comprising a **racemic** or optically pure sibutramine metabolite, or a pharmaceutically acceptable salt, solvate, or clathrate thereof, in combination with a 5-HT.sub.1A receptor. . . can be used in the methods and compositions of the invention include, but are limited to: alprenolol; WAY 100135; spiperone; **pindolol**; (S)-UH-301; penbutolol; propranolol; tertatolol; a compound of the formula I as disclosed in U.S. Pat. No. 5,552,429, which is incorporated. . .

SUMM Disorders that can be treated or prevented using a **racemic** or optically pure sibutramine metabolite, or a pharmaceutically acceptable salt, solvate, or clathrate thereof, in combination with a .beta.-adrenergic antagonist include, but are not limited to, post myocardial infarction depression. Specific .beta.-adrenergic antagonists include, but are not limited to, S(-)-**pindolol**, penbutolol, and propranolol.

SUMM

alprazolam;	quazepam;	alprenolol;
brotizolam;	temazepam;	WAY 100135;
chlordiazepoxide;	triazolam;	spiperone;
clobazam;	chlorpromazine;	S(-)-**pindolol**;
clonazepam;	mesoridazine;	R(+)-**pindolol**;
clorazepate;	thioridazine;	**racemic pindolol**;
demoxepam;	acetophenazine;	(S)-UH-301;
diazepam;	fluphenazine;	penbutolol;
estazolam;	perphenazine;	propranolol;
flumazenil;	trifluoperazine;	tertatolol;
flurazepam;	chlorprothixene;	desipramine;
halazepam;	thiothixene;	clonidine;
lorazepam;	clozapine;. . .	

L13 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1983:294157 BIOSIS

DN BA76:51649

TI ALPHA-2 ADRENERGIC RECEPTOR IN INTESTINAL EPITHELIAL CELLS IDENTIFICATION BY TRITIUM LABELED YOHIMBINE AND FAILURE TO INHIBIT CYCLIC AMP ACCUMULATION.

AU NAKAKI T; NAKADATE T; YAMAMOTO S; KATO R

CS DEP. OF PHARMACOL., KEIO UNIV. SCH. OF MED., 35 SHINANOMACHI, SHINJUKU-KU, TOKYO 160, JPN.

SO MOL PHARMACOL, (1983) 23 (1), 228-234.
CODEN: MOPMA3. ISSN: 0026-895X.

FS BA; OLD

LA English

AB .alpha.2-Adrenergic receptors in isolated rat intestinal epithelial cells were identified by using the .alpha.2-selective antagonist [3H]yohimbine. The contamination of .alpha.2-adrenergic receptors in presynaptic nerve endings was ruled out by EM observations. The [3H]yohimbine binding to the 100,000 .times. g pellet from the epithelial cells was saturable and of high affinity. Scatchard analysis yielded a Kd of 6.0 nM with a Bmax [maximum binding] of 37 fmoles of sites/mg protein. The binding was rapid

and reversible. No cooperative interactions among the binding sites were observed. Inhibition of yohimbine binding by adrenergic agonists yielded the .alpha.2-adrenergic potency series: clonidine > (.+-.)-nordefrin > (-)-norepinephrine > (-)-epinephrine .mchgt. methoxamine > (-)-phenylephrine >>> (-)-isoproterenol. (-)-Isomers were more potent than (+)-isomers. The antagonist potency series also showed .alpha.2-adrenergic specificity: yohimbine > dihydroergocryptine .mchgt. prazosin > phenoxybenzamine > propranolol. The inhibition potencies of [3H]yohimbine binding by .alpha.2-adrenergic agonists were correlated with those of the same agents for antidiarrheal effects in vivo. Clonidine (1 .mu.M) failed to reduce the cAMP levels augmented by prostaglandin E1 (PGE1) (30 .mu.M) or vasoactive intestinal peptide in the presence of 3-isobutyl-1-methyl-xanthine in these isolated cells. Epinephrine (10 .mu.M) in the absence or presence of pindolol (10 .mu.M) did not reduce the PGE1-augmented cAMP levels. The intestinal epithelial cells evidently contain .alpha.2-adrenergic receptors through which .alpha.2-adrenergic agonists may exert their antidiarrheal effect. The antidiarrheal effect of .alpha.2-adrenergic agonists may not be due to the inhibition of adenylate cyclase in these cells.

IT Miscellaneous Descriptors
RAT CLONIDINE PRAZOSIN **RACEMIC** NORDEFRIN PHENOXYBENZAMINE LEVO NOREPINEPHRINE PROPRANOLOL LEVO EPINEPHRINE METHOXAMINE LEVO PHENYLEPHRINE LEVO ISOPROTERENOL DI HYDRO ERGOCRYPTINE **PINDOLOL** AUTONOMIC-DRUG PROSTAGLANDIN E-1 EPINEPHRINE HORMONE-DRUG **GASTROINTESTINAL**-DRUG ANTI DIARRHEAL PHARMACODYNAMICS

=> FIL REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	26.75	153.21

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.56

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STRUCTURE FILE UPDATES: 26 DEC 2001 HIGHEST RN 378741-70-9
DICTIONARY FILE UPDATES: 26 DEC 2001 HIGHEST RN 378741-70-9

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

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Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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=> s pindolol/cn
L14           1 PINDOLOL/CN

=> d l14

L14  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2001 ACS
RN   13523-86-9  REGISTRY
CN   2-Propanol, 1-(1H-indol-4-yloxy)-3-[(1-methylethyl)amino]- (9CI)  (CA
     INDEX NAME)
OTHER CA INDEX NAMES:
CN   2-Propanol, 1-(indol-4-yloxy)-3-(isopropylamino)- (8CI)
OTHER NAMES:
CN   (.+-.)-4-[2-Hydroxy-3-(isopropylamino)propoxy]indole
CN   (.+-.)-LB 46
CN   (.+-.)-Pindolol
CN   (RS)-Pindolol
CN   1-[(1-Methylethyl)amino]-3-(4-indolyloxy)-2-propanol
CN   4-(2-Hydroxy-3-isopropylaminopropoxy)indole
CN   4-(3-Isopropylamino-2-hydroxypropoxy)indole
CN   Carvisken
CN   DL-4-[2-Hydroxy-3-(isopropylamino)propoxy]indole
CN   DL-LB 46
CN   DL-Pindolol
CN   dl-Pindolol
CN   LB 46
CN   Pindolol
CN   Prinodolol
CN   Visken
FS   3D CONCORD
DR   21870-06-4
MF   C14 H20 N2 O2
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       CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGPAT, DRUGU,
       EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS,
       NIOSHTIC, PHAR, PROMT, RTECS*, SPECINFO, TOXCENTER, TOXLIT, USAN,
       USPATFULL, VETU
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     Other Sources:   EINECS**, WHO
         (**Enter CHEMLIST File for up-to-date regulatory information)
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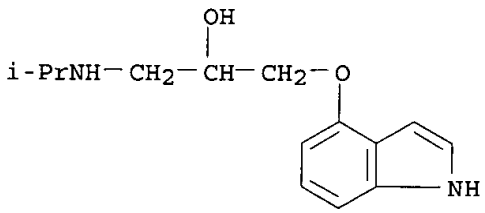


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

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              13 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
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1663 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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L15           0 RACEMIC PINDOLOL/CN

=> s s(-) pindolol
MISSING OPERATOR 'S(-'

=> s s pindolol
       1243504 S
            32 PINDOLOL
L16          1 S PINDOLOL
                 (S(W)PINDOLOL)

=> d l16

L16  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2001 ACS
RN   26328-11-0  REGISTRY
CN   2-Propanol, 1-(1H-indol-4-yloxy)-3-[(1-methylethyl)amino]-, (2S)- (9CI)
     (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   2-Propanol, 1-(1H-indol-4-yloxy)-3-[(1-methylethyl)amino]-, (S)-
CN   2-Propanol, 1-(indol-4-yloxy)-3-(isopropylamino)-, (-)- (8CI)
OTHER NAMES:
CN   (-)-Pindolol
CN   (S)-(-)-Pindolol
CN   l-Pindolol
CN   S-Pindolol
FS   STEREOSEARCH
MF   C14 H20 N2 O2
CI   COM
LC   STN Files:   ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA,
       CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CIN, CSCHEM, DRUGPAT, IFICDB,
       IFIPAT, IFIUDB, IPA, PROMT, TOXCENTER, TOXLIT, USPATFULL
         (*File contains numerically searchable property data)

Absolute stereochemistry.
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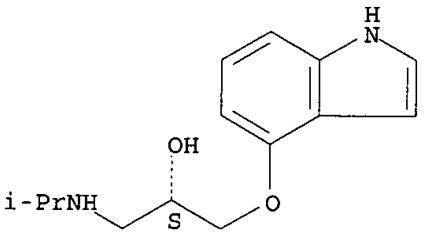


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            32 PINDOLOL
L17          1 RS PINDOLOL
                 (RS(W)PINDOLOL)

=> d l17

L17  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2001 ACS
RN   13523-86-9  REGISTRY
CN   2-Propanol, 1-(1H-indol-4-yloxy)-3-[(1-methylethyl)amino]- (9CI)  (CA
     INDEX NAME)
OTHER CA INDEX NAMES:
CN   2-Propanol, 1-(indol-4-yloxy)-3-(isopropylamino)- (8CI)
OTHER NAMES:
CN   (.+-.)-4-[2-Hydroxy-3-(isopropylamino)propoxy]indole
CN   (.+-.)-LB 46
CN   (.+-.)-Pindolol
CN   (RS)-Pindolol
CN   1-[(1-Methylethyl)amino]-3-(4-indolyloxy)-2-propanol
CN   4-(2-Hydroxy-3-isopropylaminopropoxy)indole
CN   4-(3-Isopropylamino-2-hydroxypropoxy)indole
CN   Carvisken
CN   DL-4-[2-Hydroxy-3-(isopropylamino)propoxy]indole
CN   DL-LB 46
CN   DL-Pindolol
CN   dl-Pindolol
CN   LB 46
CN   Pindolol
CN   Prinodolol
CN   Visken
FS   3D CONCORD
DR   21870-06-4
MF   C14 H20 N2 O2
CI   COM
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS,
BIOSIS,
       BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGPAT, DRUGU,
       EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS,
       NIOSHTIC, PHAR, PROMT, RTECS*, SPECINFO, TOXCENTER, TOXLIT, USAN,
       USPATFULL, VETU
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**, WHO
         (**Enter CHEMLIST File for up-to-date regulatory information)
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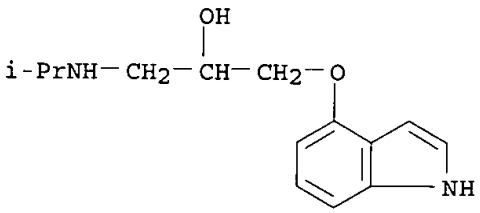


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

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            13 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
          1663 REFERENCES IN FILE CAPLUS (1967 TO DATE)


=> FIL MEDLINE, BIOSIS, CA, CAPLUS, CAOLD, EMBASE, USPATFULL, PROMT
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    27.92     181.13

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                     0.00      -0.56

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=> d his

     (FILE 'HOME' ENTERED AT 19:05:05 ON 27 DEC 2001)

     FILE 'MEDLINE, BIOSIS, CA, CAPLUS, CAOLD, EMBASE, USPATFULL, PROMT'
     ENTERED AT 19:05:16 ON 27 DEC 2001
L1          159 S 5HT1A ANTAGONIST OR 5HT1A PARTIAL AGONIST
L2          435 S 5HT1A (S) ANTAGONIST OR 5HT1A (S) PARTIAL AGONIST
L3        29438 S ?PINDOLOL
L4       794460 S GASTROINTESTINAL OR GI OR ULCER OR DUODENAL OR DYSPEPSIA OR
I
L5        10475 S CHEMOTHERAPY (S) NAUSEA
L6       803310 S L4 OR L5
L7       794460 S L6 AND L4
L8           17 S L7 AND L2
L9           14 DUP REM L8 (3 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 19:17:14 ON 27 DEC 2001
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     FILE 'HOME' ENTERED AT 19:17:55 ON 27 DEC 2001

     FILE 'MEDLINE, BIOSIS, CA, CAPLUS, CAOLD, EMBASE, USPATFULL, PROMT'
     ENTERED AT 19:20:42 ON 27 DEC 2001
L10          100 S RACEMIC PINDOLOL
L11          255 S RACEMIC (S) PINDOLOL
L12            2 S L4 AND L11
L13            2 DUP REM L12 (0 DUPLICATES REMOVED)

     FILE 'REGISTRY' ENTERED AT 19:22:58 ON 27 DEC 2001
L14            1 S PINDOLOL/CN
L15            0 S RACEMIC PINDOLOL/CN
L16            1 S S PINDOLOL
L17            1 S RS PINDOLOL

     FILE 'MEDLINE, BIOSIS, CA, CAPLUS, CAOLD, EMBASE, USPATFULL, PROMT'
     ENTERED AT 19:24:23 ON 27 DEC 2001

=> s l14 or l16 or l17
L18        18365 L14 OR L16 OR L17

=> s l4 and l18
L19          336 L4 AND L18

=> s l19 and l2
L20            0 L19 AND L2

=> s l19 and l5
L21            0 L19 AND L5

=> s gastrointestinal/ti
L22        87494 GASTROINTESTINAL/TI

=> s l22 and l19
L23            6 L22 AND L19

=> dup rem
ENTER L# LIST OR (END):l23
DUPLICATE IS NOT AVAILABLE IN 'CAOLD'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L23
L24            4 DUP REM L23 (2 DUPLICATES REMOVED)

=> d l24 1-4 bib, ab, kwic

L24  ANSWER 1 OF 4  EMBASE  COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN   2000178800  EMBASE
TI   Caco-2 cell permeability vs human gastrointestinal absorption:
     QSPR analysis.
AU   Ren S.; Lien E.J.
CS   S. Ren, Department Pharmaceutical Sciences, School of Pharmacy,
University
     of Southern California, 1985 Zonal Ave., Los Angeles, CA 90033, United
     States
SO   Progress in Drug Research, (2000) 54/- (1-23).
     Refs: 35
     ISSN: 0071-786X  CODEN: FAZMAE
CY   Switzerland
DT   Journal; Article
```

FS 030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB The aim of this study is to elucidate quantitative structure-permeability relationship (QSPR) of various organic molecules through Caco-2 cells, and to ascertain the relationship between **gastrointestinal** (**GI**) absorption in humans and Caco-2 cell permeability. Caco-2 cell permeability and human **GI** absorption data were obtained from the literature. The maximum hydrogen bond-forming capacity corrected for intra-molecular H-bonding (H(b)(c)) and Lien's QSAR model were used in this study. The latest CQSAR software was utilized in calculating the logarithm of partition coefficient in octanol/water (Clog P) and in deriving all regression equations. For 51 compounds, a significant correlation was obtained between Caco-2 cell permeability (log P(caco-2)) and H(b)(C), octanol/PBS (phosphate buffered saline, pH 7.4) distribution coefficient (log D(oct)), log MW and an indicator variable (I) for the charge, with a correlation coefficient of 0.797. When these compounds were divided into three subgroups, namely neutral, cationic and anionic compounds, much better correlations (r = 0.968, 0.915 and 0.931, respectively) were obtained using different combinations of various physicochemical parameters. A plot of human **GI** absorption vs. Caco-2 cell permeability obtained from different laboratories reveals that Caco-2 cell permeability cannot be used to precisely predict human **GI** absorption for compounds with P(caco-2) below 5 x 10-6 cm/s, due to interlaboratory and experimental variabilities, and the lack of a simple correlation between human **GI** absorption and Caco-2 cell permeability. Caco-2 cell permeability may be estimated from the structures of drug molecules using the above-mentioned physicochemical parameters. In general, for compounds with P(caco-2) above 5 x 10-6 cm/s, human **GI** absorption ranges from 50 to 100%. This is generally acceptable for development into oral dosage form. For the compounds with P(caco-2) below 5 x 10-6 cm/s, careful interpretation of caco-2 cell permeability and use of internal standard for comparison are recommended. Otherwise, good drug candidates may be excluded due to incorrectly predicted poor absorption.
TI Caco-2 cell permeability vs human **gastrointestinal** absorption: QSPR analysis.
AB . . . is to elucidate quantitative structure-permeability relationship (QSPR) of various organic molecules through Caco-2 cells, and to ascertain the relationship between **gastrointestinal** (**GI**) absorption in humans and Caco-2 cell permeability. Caco-2 cell permeability and human **GI** absorption data were obtained from the literature. The maximum hydrogen bond-forming capacity corrected for intra-molecular H-bonding (H(b)(c)) and Lien's QSAR. . . (r = 0.968, 0.915 and 0.931, respectively) were obtained using different combinations of various physicochemical parameters. A plot of human **GI** absorption vs. Caco-2 cell permeability obtained from different laboratories reveals that Caco-2 cell permeability cannot be used to precisely predict human **GI** absorption for compounds with P(caco-2) below 5 x 10-6 cm/s, due to interlaboratory and experimental variabilities, and the lack of a simple correlation between human **GI** absorption and Caco-2 cell permeability. Caco-2 cell permeability may be estimated from the structures of drug molecules using the above-mentioned physicochemical parameters. In general, for compounds with P(caco-2) above 5 x 10-6 cm/s, human **GI** absorption ranges

from 50 to 100%. This is generally acceptable for development into oral dosage form. For the compounds with. . .

CT Medical Descriptors:
*cell strain CACO 2
cell membrane permeability
computer analysis
drug absorption
gastrointestinal absorption
hydrogen bond
partition coefficient
physical chemistry
quantitative structure activity relation
regression analysis
structure activity relation
human
human cell
article
priority journal
alprenolol: PK, pharmacokinetics
alprenolol: PD, pharmacology
aminophenazone: PK, pharmacokinetics
aminophenazone: PD,. . .

RN. . . 50-23-7; (indometacin) 53-86-1, 74252-25-8, 7681-54-1; (meloxicam) 71125-38-7; (metoprolol) 37350-58-6; (nevirapine) 129618-40-2; (nicotine) 54-11-5; (phencyclidine) 77-10-1, 956-90-1; (phenytoin) 57-41-0, 630-93-3;
(pindolol) **13523-86-9**, **21870-06-4**; (piroxicam) 36322-90-4; (progesterone) 57-83-0; (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6; (salicylic acid) 63-36-5, 69-72-7; (scopolamine) 138-12-5, 51-34-3, 55-16-3; (telmisartan) 144701-48-4;. .
.

L24 ANSWER 2 OF 4 MEDLINE
AN 97344708 MEDLINE
DN 97344708 PubMed ID: 9201075
TI Distribution of beta-adrenoceptor subtypes in **gastrointestinal** tract of nondiabetic and diabetic BB rats. A longitudinal study.
AU Yu O; Ouyang A
CS Division of Gastroenterology, Hospital of the University of Pennsylvania, Philadelphia 19104, USA.
NC RO1 DK-34148 (NIDDK)
SO DIGESTIVE DISEASES AND SCIENCES, (1997 Jun) 42 (6) 1146-53.
Journal code: EAD; 7902782. ISSN: 0163-2116.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199707
ED Entered STN: 19970724
Last Updated on STN: 19970724
Entered Medline: 19970716
AB The effects of aging and diabetes on the distribution of beta-adrenoceptor
subtypes in the gut were investigated in the BB rat. [125I]Cyanopindolol binding to 10-micron sections was evaluated using film autoradiography. Cyanopindolol binding to beta-, beta 1-, and beta 2-adrenoceptors was displaced by 1 microM propranolol, 50 nM ICI-89-406, and 100 nM ICI-118-551, respectively. beta-Adrenoceptor binding was highest in the circular muscle of proximal colon and lowest in the pylorus of 4- to 5-month-old rats. Aging (8- to 10-month-old vs. 4- to 5-month-old rats)

was associated with increased beta-adrenoceptor binding in the pylorus and reduced binding in the proximal colon. Diabetes had a time-dependent effect on the level of beta-adrenoceptor binding. It was increased in the antral and pyloric stomach but longer periods of diabetes caused a reduction in beta-adrenoceptor binding in the pylorus. Those in the intestine were reduced time-dependently and involved beta 1- or beta 2-adrenoceptors or both.

TI Distribution of beta-adrenoceptor subtypes in **gastrointestinal** tract of nondiabetic and diabetic BB rats. A longitudinal study.

CT . . . U.S. Gov't, P.H.S.
Adrenergic beta-Antagonists: PD, pharmacology
*Aging: ME, metabolism
*Diabetes Mellitus, Experimental: ME, metabolism
*Diabetes Mellitus, Insulin-Dependent: ME, metabolism
***Gastrointestinal System: ME, metabolism**
Pindolol: AA, analogs & derivatives
Pindolol: PD, pharmacology
Rats
Rats, Inbred BB
Receptors, Adrenergic, beta: DE, drug. . .

RN **13523-86-9 (Pindolol)**; 81608-27-7 (cyanopindolol)

L24 ANSWER 3 OF 4 CA COPYRIGHT 2001 ACS DUPLICATE 1

AN 125:230385 CA

TI Effect of liquid meal on **gastrointestinal** transit time of the oral dosage form in dogs

AU Nishiyama, T.; Suda, M.; Seki, M.; Sugawara, S.; Miyajima, M.; Kawasaki, C.; Otagiri, M.

CS Central Research Laboratories, Zeria Pharmaceutical Co., Ltd., Saitama, 360-01, Japan

SO Proc. Int. Symp. Controlled Release Bioact. Mater. (1996), 23rd, 581-582
CODEN: PCRMEY; ISSN: 1022-0178

DT Journal

LA English

AB Continuous and weak contractions obsd. following the intake of a liq. meal brought about a delay in gastric emptying time (GET). However, inter- and intra-individual variations in GET and gastric motor activities were relatively small after a liq. meal compared with variations under the other 2 conditions. Results suggested that bioavailability studies which utilize intake of liq. meals in dogs will be useful for evaluating the in vivo performance of oral controlled-release dosage forms.

TI Effect of liquid meal on **gastrointestinal** transit time of the oral dosage form in dogs

ST oral controlled release dosage **gastrointestinal** transit

IT Digestive tract
Drug bioavailability
Drug interactions
(liq. meal effect on **gastrointestinal** transit time of oral dosage forms in dog)

IT Pharmaceutical dosage forms
(oral, controlled-release, liq. meal effect on **gastrointestinal** transit time of oral dosage forms in dog)

IT 103-90-2, Acetaminophen **13523-86-9**, Pindolol
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(liq. meal effect on **gastrointestinal** transit time of oral dosage forms in dog)

L24 ANSWER 4 OF 4 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 89273969 EMBASE
DN 1989273969
TI Drug absorption in **gastrointestinal** disease and surgery.
AU Gubbins P.O.; Bertch K.E.
CS Division of Clinical Practice, College of Pharmacy, University of Kentucky
Medical Center, Lexington, KY, United States
SO Pharmacotherapy, (1989) 9/5 (285-295).
ISSN: 0277-0008 CODEN: PHPYDQ
CY United States
DT Journal
FS 030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB It is well recognized that drug absorption from the **gastrointestinal** tract is influenced by gastric and intestinal motility, surface area available for absorption, and physicochemical properties of the drug. Disease and surgery have been shown to alter these factors. Consequently, drug absorption can be altered as well, and these affect drug therapy. Apparently this effect is variable, but the variability may be due in part to the complexities of performing studies in this area. For example, many patient factors as well as drug characteristics must be considered. In addition, appropriate interpretation of results requires that intravenous data be collected if changes in absorption are based on bioavailability. At this time, the alterations in drug absorption due to **gastrointestinal** disease and surgery are of unknown or little clinical significance; nevertheless, clinicians should be aware that the possibility of malabsorption exists and anticipate any monitoring of or alterations in therapy that may have to be made.
TI Drug absorption in **gastrointestinal** disease and surgery.
AB It is well recognized that drug absorption from the **gastrointestinal** tract is influenced by gastric and intestinal motility, surface area available for absorption, and physicochemical properties of the drug. Disease. . . be collected if changes in absorption are based on bioavailability. At this time, the alterations in drug absorption due to **gastrointestinal** disease and surgery are of unknown or little clinical significance; nevertheless, clinicians should be aware that the possibility of malabsorption. . .
CT Medical Descriptors:
*celiac disease
*crohn disease
*drug absorption
***gastrointestinal surgery**
*ulcerative colitis
review
human
oral drug administration
priority journal
*antibiotic agent
*corticosteroid
*cyclosporin
*digoxin
*indometacin
*methyldopa
*metronidazole

```
     *paracetamol
     *pindolol
     *propranolol
     *salicylic acid
     *tetracycline
     *warfarin
RN   (cyclosporin) 79217-60-0; (digoxin) 20830-75-5, 57285-89-9; (indometacin)
     53-86-1, 74252-25-8, 7681-54-1; (methyldopa) 555-29-3, 555-30-6;
     (metronidazole) 39322-38-8, 443-48-1; (paracetamol) 103-90-2; (pindolol)
     13523-86-9, 21870-06-4; (propranolol) 13013-17-7,
     318-98-9, 3506-09-0, 4199-09-1, 525-66-6; (salicylic acid) 63-36-5,
     69-72-7; (tetracycline) 23843-90-5, 60-54-8, 64-75-5; (warfarin)
129-06-6,
     2610-86-8, 3324-63-8, 5543-58-8, 81-81-2


=> d his

     (FILE 'HOME' ENTERED AT 19:05:05 ON 27 DEC 2001)

     FILE 'MEDLINE, BIOSIS, CA, CAPLUS, CAOLD, EMBASE, USPATFULL, PROMT'
     ENTERED AT 19:05:16 ON 27 DEC 2001
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L2          435 S 5HT1A (S) ANTAGONIST OR 5HT1A (S) PARTIAL AGONIST
L3        29438 S ?PINDOLOL
L4       794460 S GASTROINTESTINAL OR GI OR ULCER OR DUODENAL OR DYSPEPSIA OR
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L5        10475 S CHEMOTHERAPY (S) NAUSEA
L6       803310 S L4 OR L5
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L19         336 S L4 AND L18
L20           0 S L19 AND L2
L21           0 S L19 AND L5
L22       87494 S GASTROINTESTINAL/TI
L23           6 S L22 AND L19
L24           4 DUP REM L23 (2 DUPLICATES REMOVED)
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